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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,171	07/01/2003	Carol A. Tosaya	D-02017A	5208

7590 09/05/2007

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EXAMINER	
KISH, JAMES M	

ART UNIT	PAPER NUMBER
3737	

MAIL DATE	DELIVERY MODE
09/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/612,171	TOSAYA ET AL.	
	Examiner	Art Unit	
	James Kish	3737	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-96* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-43,49-66,69,71-79,81-86 and 88-96* is/are rejected.

7)☒ Claim(s) *44-48,67,68,70,80 and 87* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments with respect to claims 1-96 have been considered but are moot in view of the new ground(s) of rejection.

2. Examiner notes that Applicant has considered and respectfully declined to file a Terminal Disclaimer with regard to the Double Patenting rejection presented in the previous Office Action. However, this rejection still holds and has therefore been repeated below in the current Office Action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1-96 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-17, and 20-99 of U.S. Patent Application No. 2005/0020945. Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions disclose opening of a blood brain barrier to allow transference of compounds, whether it be CSF or a treatment agent, through the barrier using a similar, if not identical, apparatus.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-6, 11-16, 21-36, 39-42, 49-56, 58, 60, 62-66, 69, 71-76, 78-79, 81-86, 88-90 and 92-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jolesz et al. (US Patent No. 5,752,515) in view of Chalifour et al. (US Patent App. 2004/0006092). Jolesz discloses a method and apparatus for treating neurological disorders by ultrasonic delivery of compounds through the blood-brain barrier (BBB). See column 3, lines 44-67. The ultrasound is applied through the skull itself via a phased array of transducers, a focused ultrasound transducer or a combination of ultrasound source and an acoustic lens, placed outside the skull (column 2, line 66 through column 3, line 37). The ultrasound can be focused electronically or

mechanically (column 5, lines 33-41). Discussion of cavitation can be found throughout the reference, and particularly at column 5, line 64 through column 6, line 27. The invention allows for both continuous wave or burst (pulsed) mode operation (column 6, line 24). The device uses image-based localization of the region. Such images can be obtained on the devices described at column 6, lines 38-61. The effects of the skull bone are incorporated to allow the ultrasound to focus at a common location (column 7, lines 33-51). Jolesz does not explicitly state that one such disease to be treated is Alzheimer's or any other protein-related disease, however, Alzheimer's Disease (AD) is a neurological, mental and behavioral disorder, and a known protein-related disease and therefore is incorporated into the possible disorders that are treatable by Jolesz as disclosed at column 3, lines 60-67). Chalifour teaches a method of treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amount of an amidine compound. The compound is used to, among other things, at least prevent, slow or stop deterioration of cognitive function in a patient (paragraph 75). It would have been obvious to one having ordinary skill in the art at the time the invention was made to incorporate the compounds of Chalifour into the method and system of Jolesz to treat amyloid-related diseases. Furthermore, Chalifour teaches several methods to pass the compound through the BBB and it would be obvious to one of skill in the art to combine the teaches of Chalifour and Jolesz in order to provide a more accurate entry port for the compound through the barrier.

With respect to the specific limitation of the independent claims, Jolesz provides an ultrasound emitter that will provide acoustic energy to a localized portion of the BBB.

Therefore, the energy will indirectly enter the brain or neurological region which has been, is or is expected to potentially be subject to the abnormal bodies. The ultrasound will be emitted with a desired characteristic, i.e. in a controlled manner. The compound of Chalifour will then at least prevent, slow or stop deterioration of cognitive function in a patient.

5. Claims 1, 7-10, 17-20, 41, 43, 59, 61, 77, 88 and 91 rejected under 35 U.S.C. 103(a) as being unpatentable over Brisken et al. (US Patent No. 6,464,680) in view of Chalifour et al. Brisken discloses a method of enhancing cellular absorption of a substance delivered into a target region with the use of vibrational energy to the target region (see Abstract). The invention can be used in treatment of abnormalities of the brain (column 12, lines 4-14) by allowing treatment to brain cells protected by the blood-brain barrier (column 1, lines 54-55). In one embodiment, an injection needle and the ultrasound energy emitter are located on the end of a catheter and can be introduced through a blood vessel or other luminal cavity (column 3, lines 4-28). The ultrasound conditions induce a preferred cellular response that increases porosity and subsequent uptake of therapeutic agents (column 5, line 55 through column 6, line 8). See column 7, lines 43-55 for possible effects of drugs. The wave may be divergent or focused on a small spot with the resolution of the ultrasonic emitter device (column 9, lines 65-67 and column 11, lines 54-63). Column 5, lines 38-54 discuss the thermal index of the vasculature immediately around the device. It is monitored based on the equation found at line 43. Chalifour teaches a method of treating or preventing an amyloid-

related disease in a subject comprising administering to the subject a therapeutic amount of an amidine compound. The compound is used to, among other things, at least prevent, slow or stop deterioration of cognitive function in a patient (paragraph 75). It would have been obvious to one having ordinary skill in the art at the time the invention was made to incorporate the compounds of Chalifour into the method and system of Brisken to treat amyloid-related diseases. Furthermore, Chalifour teaches several methods to pass the compound through the BBB and it would be obvious to one of skill in the art to combine the teaches of Chalifour and Brisken in order to provide a more accurate entry port for the compound through the barrier.

6. Claims 37-38, 57 and 92 rejected under 35 U.S.C. 103(a) as being unpatentable over Jolesz et al in view of Hynynen et al (US Patent No. 6,514,221), further in view of Chalifour et al. Jolesz discloses a method and apparatus for treating neurological disorders by ultrasonic delivery of compounds through the blood-brain barrier (BBB). However, while cavitation is discussed by Jolesz, the compounds delivered through the BBB are not explicitly cavitation aiding agents. Hynynen teaches a method of opening the blood-organ barrier of a subject providing an exogenous agent (see Abstract). The agent is described as having microbubbles or solid particles contained within that will vaporize via body heat or ultrasonic energy (see all of column 5, as well as column 6, lines 1-43). There is also a measure of the temperature elevation due to the sonication (column 9, line 65 through column 10, line 12). Hynynen also discusses non-focused ultrasound at column 10, lines 36-57. It would have been obvious to one having

ordinary skill in the art at the time the invention was made to incorporate a cavitation inducing contrast agent as taught by Hynynen into the system of Jolesz in order to allow opening of the BBB at low enough energy levels so as not to induce thermal damage (see Abstract).

Chalifour teaches a method of treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amount of an amidine compound. The compound is used to, among other things, at least prevent, slow or stop deterioration of cognitive function in a patient (paragraph 75). It would have been obvious to one having ordinary skill in the art at the time the invention was made to incorporate the compounds of Chalifour into the method and system of Jolesz to treat amyloid-related diseases. Furthermore, Chalifour teaches several methods to pass the compound through the BBB and it would be obvious to one of skill in the art to combine the teaches of Chalifour and Jolesz in order to provide a more accurate entry port for the compound through the barrier.

Allowable Subject Matter

7. Claims 44-48, 67-68, 70, 80 and 87 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James Kish whose telephone number is 571-272-5554. The examiner can normally be reached on 8:30 - 5:00 ~ Mon. - Fri..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Casler can be reached on 571-272-4956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JMK

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